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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,253	06/02/2006	Helen Francis-Lang	05-967-A5	4136

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MCDONNELL BOEHNEN HULBERT @ BERGHOFF LLP
300 SOUTH WACKER DRIVE
SUITE 3100
CHICAGO, IL 60606

EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,253	FRANCIS-LANG ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8-10 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8-10 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 22, 2009 has been entered.

Status of Claims

Claims 1, 8-10, and 26 are pending and under examination on the merits in the instant case.

Response to Arguments

Applicant's arguments with respect to claims 1, 8-10, and 26 filed with the RCE have been fully considered but are moot in view of the new ground of rejection. See below.

Claim Objections

Claim 8 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 8 depends from claim 1. Claim 8 recites two limitations: 1) the assay system includes an expression assay comprising a UP nucleic acid and 2) the candidate test agent is a nucleic acid modulator. It is found that claim

1 already requires "an assay system comprising a uridine phosphorylase (UP) nucleic acid" (see step "(a)") and "determining the expression of UP nucleic acid" (see step "(c)"). As such, the method of claim 1 necessarily comprises an assay system that "includes an expression assay comprising a UP nucleic acid" as claimed in claim 8, which thus does not further limit the subject matter of claim 1. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 10 is objected to because of the following informalities: Claim 10 is currently written to depend from claim 8. Claim 10 recites that the nucleic acid modulator is a PMO. As applicant must be aware, and as evidenced by the disclosure of the instant specification (see page 18: "the antisense oligomer is a phosphothioate morpholino oligomer (PMO)"), the claimed PMO in and of itself is not a nucleic acid modulator. Instead, the PMO is a modified "antisense" oligonucleotide. As such, it appears that claim 10 should be written to depend from claim 9 for appropriate characterization of the PMO such that it is consistent with the art-accepted knowledge as well as the disclosure of the instant specification. Appropriate correction is required. For examination purpose, the PMO claimed in claim 10 will be interpreted to mean an antisense PMO.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 8-10, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deneen et al. (*Cancer Research,* 2003, 63:4268-4274) in view of Monga et al. (*Gastroenterology,* 2003, 124:202-216) and Verma et al. (*Clinical Cancer Research,* 2003, 9:1291-1300).

Deneen et al. suggest that "uridine phosphorylase contributes to pathways that initiate cellular proliferation" and that "uridine phosphorylase is promoting cellular transformation by impacting other physiological mechanisms directly linked to cellular proliferation or survival". See page 4273, right column. Deneen et al. do not teach identifying a "candidate" beta-catenin pathway modulating agent based on the changed expression level of uridine phosphorylase.

Monga et al. teach that the Wnt signaling pathway involving beta-catenin regulates cellular proliferation and that an antisense PMO targeted to beta-catenin, a key component of the Wnt pathway, decreases cellular proliferation compared to a mismatch control PMO. See the entire reference.

Consistent with Monga et al., Verma et al. teach that the Wnt/beta-catenin signaling pathway regulates cellular proliferation/growth. Verma et al. also teach that an siRNA targeted to beta-catenin inhibits cellular proliferation whereas mock transfection does not affect beta-catenin expression or activity. See the entire reference.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an antisense PMO or an siRNA against uridine phosphorylase, wherein the antisense PMO or siRNA functions as a "candidate" agent that is likely to inhibit cellular proliferative activity mediated by beta-catenin in the Wnt/beta-catenin signaling pathway.

Note that "the words of the claim must be given their plain meaning unless the plain meaning is inconsistent with the specification." See MPEP 2111.01. The dictionary-based, plain meaning of the word "candidate" recited in the claims in the instant case is "one ***likely or suited to*** undergo or ***be chosen for something specified***" (emphasis added). See the attached dictionary citation. Applicant's attention is also directed to the fact that the instant specification does not disclose the meaning of the word "candidate", nor does it provide any indication that the word "candidate" is used in a particular context that is different from the plain English meaning.

As clearly set forth in the teachings of Monga et al. and Verma et al., making and using beta-catenin inhibitors (e.g., antisense PMO, siRNA) to inhibit beta-catenin expression and its activity in cellular proliferation were art-recognized goal in the art, wherein the beta-catenin expression is inhibited only in the presence of the inhibitors, but not in the presence of a negative control (e.g., mismatch control or mock transfection). As such, given the plain meaning of the claim language, further in view of the totality of the teachings of the prior art cited herein, it would have been apparent to one of ordinary skill in the art that identifying other "candidate"

antisense PMO or siRNA compounds such as those targeted to uridine phosphorylase that was suggested to participate in and contribute to the beta-catenin-mediated cell proliferation pathway (see Deneen et al.), wherein such compounds are "likely" to inhibit beta-catenin activity (e.g., cell proliferation) would have appeared useful for inhibiting beta-catenin-mediated cell proliferative activity. Note that for obviousness under §103, "all that is required is a reasonable expectation of success", and it does not require "absolute predictability of success". See *In re O 'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988) at 1681. Since the likelihood of the functional role of uridine phosphorylase in participating in or influencing the Wnt/beta-catenin signaling pathway for promoting cellular proliferation was reasonably, if not absolutely, established in the art as suggested by Deneen et al., and since the utility of antisense PMOs and siRNAs for inhibiting target-specific gene expression/activity in a cell, especially for inhibiting beta-catenin activity was known in the art as taught by Monga et al. and Verma et al., and since making a target-specific antisense PMO or siRNA that inhibits target expression only in the presence of the PMO or siRNA but not in the absence of the PMO or siRNA was within the technical grasp of one of ordinary skill in the art at the time the invention was made as evidenced by the teachings of Monga et al. and Verma et al., one of ordinary skill in the art would have had a reasonable expectation of success in identifying an antisense PMO or siRNA targeted to uridine phosphorylase that inhibits uridine phosphorylase expression only in the presence of the antisense PMO or siRNA as a "likely" or "suitable" candidate beta-catenin pathway modulating agent as claimed in the instant case. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tracy Vivlemore (Acting SPE) can be reached on 571-272-2914. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/Dana Shin/
Examiner, Art Unit 1635